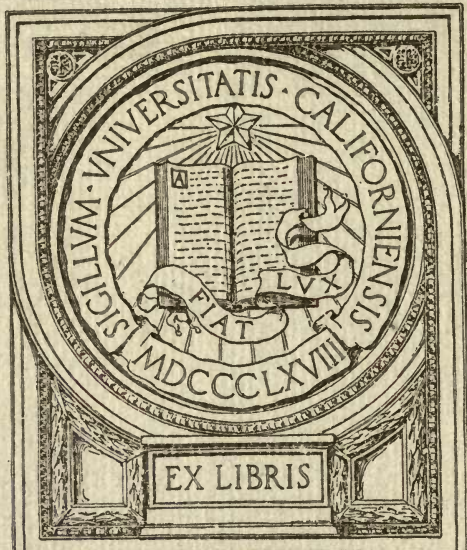

The Intra-Uterine Growth-Cycles of the Guinea-Pig.

by

J. Marion Read

With 2 diagrams

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The Intra-Uterine Growth-Cycles of the Guinea-Pig.

By

J. Marion Read.

(From the Rudolph Spreckels Physiological Laboratory of the University of California.)

With 2 diagrams.

Eingegangen am 5. November 1912.

The idea was expressed by LOEB[1]) in 1906 that some of the phenomena acompanying the early stages of development suggest that growth may be determined by an autocatalysed chemical reaction. He is inclined to believe that cell division in the developing egg ceases when the ratio of nuclear to cytoplasmic material reaches a certain limit, and expresses the belief that »This ratio is determined by the laws of mass action and equilibrium«. Following up this idea, ROBERTSON[2]) and OSTWALD[3]) published almost simultaneously in 1908 their investigations showing the great similarity between growth curves and the curves expressing the relationship between time and amount of transformation in a monomolecular autocatalytic reaction.

The work of numerous investigators has rendered available a large amount of data upon the growth of plants and animals of various species. Especially accurate data upon the growth of man have been accumulated by the British Association Anthropometric Committee and by QUETELET in Belgium. It was these data in addition to those published by DONALDSON[4]) upon the growth of rats which ROBERTSON[5]) chiefly utilized in illustrating his thesis.

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[1]) J. LOEB, »Dynamics of Living Matter.« New York 1906. p. 56 et seq.

[2]) T. B. ROBERTSON, Arch. f. Entw.-Mech. Bd. 25. 1908.

[3]) WO. OSTWALD, »Über die zeitlichen Eigenschaften der Entwicklungsvorgänge.« Vorträge u. Aufs. über Entwicklungsmech. d. Organismen, herausgeg. von WILH. ROUX. Heft 5. Juli 1908.

[4]) DONALDSON, BOAS Memorial Volume. New York 1906. p. 5.

[5]) T. B. ROBERTSON, loc. cit.

Mammals seem to have furnished the greatest amount of accurate information which we possess upon this subject, for it is an easy matter to weigh a mammal at birth and at stated times thereafter and thus to ascertain its increase in weight, which is the best measure of the growth of the whole organism. From information thus obtained, however, we get no idea of the rate of growth before birth. A curve representing this period of growth is in many respects the most important, for, if obtained, it would show the beginning of growth, the changes following upon fertilization, that is to say, the actual starting point of the reaction.

OSTWALD[1]) published curves showing the intra-uterine growth of the human foetus. These curves were constructed from the data of HIS and TOLDT in which length was taken as the measure of the rate of growth. OSTWALD also showed a curve of the prenatal growth of man based upon the weights obtained by FEHLING. Such data must, of necessity, be limited in number and consequently be insufficient for generalization, although OSTWALD's curves are remarkably smooth. So far as I am aware, this is the only information we have concerning the intra-uterine growth of any mammal.

I have observed that curves constructed from the daily weights of guinea-pigs during pregnancy were not straight but somewhat S-shaped. MINOT[2]) in his exhaustive work on growth gives a table of the weight changes of pregnant guinea-pigs. The curve constructed from his data so nearly resembled the one I obtained that the possibility occurred to me of utilizing these data for the purpose of following the course of intra-uterine growth.

That the guinea-pig is particularly suited for work upon this subject is shown:

1) In that the ratio of the weight of the litter to that of the mother is very high, the average weight of a litter of three being about 225 gms. and the average weight of the adult mothers about 740 gms. These figures give a ratio of nearly 1 : 3.

2) In that the small number in the litter is an advantage, for the weight of the unit organism is considerable, even after the weight of the litter is divided by the number born.

The ten cases considered herein were selected from eighteen or twenty available ones. They were chosen because they seemed to

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[1]) OSTWALD, loc. cit.

[2]) C. S. MINOT, Journ. of Physiol. Vol. 12. 1891.

be normal in every way. As far as possible adult mothers were chosen, and so no litters consisting of only one are included [1]). The cases designated as X_1 and K_1 were first litters, however, containig three and two respectively. No cases were included in which the mother became pregnant immediately after parturition, thus nursing one litter while carrying another.

All of my animals were weighed every second day, so there is a complete record of the weights of all for the past fifteen months. Table I, column A, gives the weights of the mothers at copulation. Except in the cases noted under »remarks« the weight is that actually observed, recorded within twenty-four hours before or after copulation. In the four cases noted under »remarks« the weight in column A was raised to an average of the weights for a week or two preceding. In most cases the weight at copulation was very close to the average weight.

For the sake of comparison and as an aid to correct valuation of the results, I am publishing two tables. Table I gives the weights as they were actually recorded and Table II shows these weights again with six of them corrected as explained under »remarks«.

It may be noted here while discussing the weights of adult guinea-pigs and the corrections I have deemed it advisable to make, that these animals display considerable variation in weight from day to day. In an adult guinea-pig of 650—850 gms. a variation of ten or twenty grams is not exceptional. MINOT [2]) says, »In all the weighings there is necessarily an error ±. A positive error because the digestive tract, particularly the wide caecum, contains always considerable quantities of undigested material; moreover the bladder may hold a greater or less quantity of urine. A negative error because every illness, even a very slight indisposition and every injury such as a bite for instance, causes a greater or less loss of weight. The quantitative value of these errors is presumably not very great; they probably counterbalance one another to a certain extent in the averages which may be accepted as approximately accurate.« Guinea-pigs are very sensitive animals and a very slight disturbance will cause considerable change in weight. At a recent weighing almost all of my animals had lost heavily due to the fact that they had been moved the day before from one animal house

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[1]) Immature mothers usually bear one in a litter.

[2]) C. S. MINOT, loc. cit.

Table I.

Actual, observed weights.

	A Weight at copulation	B Weight just before parturition	B-A Increase of weight during gestation	C Weights of the young ones in the litter	(B-A)-C Weight due to fat placentae and growth of mother	Remarks upon revision of weights, too high or too low
A_2	749	940	191	64, 67, 72	— 12	B is too low, average of weights for 16 days preceding parturition is 952 g.
A_3	810	1042	232	59, 68, 76	29	
B_3	760	1030	270	67, 92	111	
B_4	855	1110	255	80, 84, 97	— 13	A is too high, average of weights for two weeks preceding copulation being 834 g.
C_4	750	1091	341	57, 82, 95	108	A is too low, average of weights for 10 days preceding copulation being 770 g.
H_2	542	908	366	76, 77, 79	132	A is too low, average of weights for two weeks preceding copulation being 579 g.
X_1	560	881	321	64, 67, 70	120	
Bp_1	766	1090	324	72, 77, 79	96	A is too low, average of weights for two weeks preceding copulation being 783 g.
Bp_2	772	1030	258	74, 75, 79	30	B is too low, average of weights for a week preceding parturition being 1055 g.
K_1	430	715	285	79, 81	125	

into another, a distance of 50 feet perhaps. The disturbance was sufficient to cause one of the animals to give birth prematurely (59 days) to a litter of three.

The low weight at copulation in the four cases under consideration I belive to be due to the excitement and muscular work which is always attendant when a male is put into the pen with a female. The chasing is often quite severe and continues for some time. Upon many occasions I have noted a loss of weight after copulation.

Table II.

Observed weights and weights corrected.

	A Weight at copulation	B Weight just before parturition	B-A Increase of weight during gestation	C Total weight of litter	(B-A)-C Weight due to fat placentae and growth of mother	Remarks upon revision of weights, too high or too low
A_2	730	955	225	203	22	A observed (749) was too high, average for 10 days preceding was 731.
A_3	810	1042	232	203	29	
B_3	760	1030	270	159	111	
B_4	834	1110	276	261	15	
C_4	760	1091	331	233	98	Though the average for A is 770, I believe it is a little too high and that 760 represents better the weight at copulation.
H_2	575	908	333	234	99	
X_1	560	881	321	201	120	
Bp_1	783	1090	307	228	79	
Bp_2	772	1045	273	228	45	The weight parturition has not been raised to the average of 1055, for reasons discussed in the text.
K_1	430	715	285	160	125	

In only two cases was the weight in column B corrected and in both it was raised to approach an average for a week or two preceding. It sometimes happens that the mother becomes upset somewhat before birth and eats lightly, thus gaining but little or even losing weight just before parturition. In most cases there is a steady gain up to the time of birth so in the two which suffered a loss it seemed reasonable to correct the weight. It must be understood that in all cases in which the weight is corrected it has never been raised or lowered to reach the average, but a weight has been chosen between the observed and averaged weight.

In the third column of Table II the increase of weight during gestation is given. This is in every case greater than the total weight of the litter. The difference between these two figures (found

in the fifth column) represents the weight of placentae, amniotic fluid and blood lost at birth, as well as the growth of the mother. The mother's growth can be obtained separately by getting the difference between the weight at copulation and just after delivery. A figure thus obtained however, would represent two kinds of growth, namely, 1) continuous growth of the mother, and 2) fat accumulated during pregnancy. This accumulation of fat during the period of gestation seems to be a general phenomenon and is especially to be noted in the case of the guinea-pig, the milk of which contains such a high percentage of fat[1]). For our purpose, we will disregard as far as we can, everything which is not growth of young in utero; this is represented by the value in the fifth column of Table II.

Table III is an illustrative page of the calculations showing the figures for A_2, Bp_2, and K_1. The weight of the mother on every second day is placed in the first column and in the second appears the increase at each period over the weight at copulation. The last value in the second column corresponds to that in the third column of Table II.

Since we are concerned here with the increase in the weight of the litter only, it becomes necessary to eliminate the growth due to placentae and fat accumulated by the mother, in short, everything not representing the growth of the litter. We have only one determination upon the weight of the litter itself, that is, its weight just after birth. The difference between the weight of the litter and the total increase in the mother's weight during gestation is the value representing all increase in weight other than that of the litter. But this extra weight has accumulated along with the young in utero, so in eliminating it we must distribute it over the whole period of gestation. In order to eliminate this weight justly and to distribute it proportionally throughout the whole period, the following method has been adopted. A horizontal line was ruled off on coordinate paper. It represented by its length the number of days of gestation, each day being represented by one space on the paper. At the right end of this line a perpendicular was erected which corresponded in height to the value in the fifth column of Table II. Each space represented one gram. A right-angled triangle was formed when the free ends of the horizontal and perpendicular lines were joined by a straight line, which formed the hypotenuse. The distance

[1]) J. Marion Read, »Observations on the suckling period in the guinea-pig.« University of Cal. publications in Zoology. Vol. 9. pp. 342, 343.

Table III.

Illustrative page of calculations, showing complete figures obtained from three of the ten litters utilized.

Days after c op.	A_2 Weights of mother during pregnancy	Increase over weight at copulation	Corrected for weight of placentae fat and growth	Bp_2 Weights of mother during pregnancy	Increase over weight at copulation	Corrected for weight of placentae fat and growth	K_1 Weights of mother during pregnancy	Increase over weight at copulation	Corrected for weight of placentae fat and growth
	Three in the litter			Three in the litter			Two in the litter		
0	730	0	0	772	0	0	430	0	0
2	730		0	776	4	3	453	23	19
4	757	27	25	785	13	11	433	3	− 4
6	757	27	25	785	13	10	449	19	8
8	760	30	27	785	13	8	455	25	10
10	747	17	14	790	18	12	456	26	9
12	755	25	21	778	6	0	463	33	13
14	781	51	47	800	28	19	480	50	26
16				785	13	3	490	60	32
18	782	52	47	800	28	17	486	56	25
20	777	47	41	792	20	8	485	55	20
22	779	49	42	820	48	35	500	70	31
24	782	52	45	880	108	93	509	79	35
26				821	49	33	511	81	33
28	788	58	50	860	88	70	512	82	30
30	813	83	74	868	96	77	517	87	32
32	826	96	86	840	68	57	519	89	28
34	846	116	106	878	106	84			
36	848	118	107	886	114	90	570	140	75
38	870	140	128	895	123	98	584	154	85
40	875	145	133	930	158	132	575	145	73
42	883	153	140	913	141	114	580	150	74
44	915	185	172	927	155	127	585	155	75
46	908	178	164	924	152	123	592	162	79
48	918	188	173	956	184	153	618	178	91
50	944	214	199	1000	228	196	624	194	103
52	950	220	204	1007	235	202	629	199	103
54	960	230	213	1000	228	197	640	210	110
56	960	230	213	1020	248	212	655	225	120
58	985	255	237	1020	248	210	664	234	125
60	932	202	184	1010	238	199	668	238	126
62	940	210	191	1040	268	228	680	250	134
64	935	205	185	1040	268	226	684	254	135
66	945	215	195	1030	258	214	717	287	164
68	955	225	203	1045	273	228	715	285	160

from the horizontal line to the hypotenuse along the ordinates increases as we pass from left to right, and approach the perpendicular line whose length represents the weight increase during gestation, which was due to other factors than the weight of the litter. The length of each ordinate (distance between the base and hypotenuse) represents the increase in weight which is in excess of the litter's weight on that day, just as the length of the perpendicular forming one side of the triangle represents the difference *at birth* between the total increase of weight during gestation and the weight of the litter. The length of every second ordinate (i. e. every second day) was obtained, and this figure subtracted from the weight for that day in the second column of Table III. The remainder obtained was set down in the third column of Table III. It represented the weight of the litter on that day, the last figure in the column being the total weight of the litter at birth. This correction was made in all ten cases. The results are tabulated in Table IV.

This method of eliminating the weight of the deciduae, growth of the mother, and the accumulation of fat by the mother during the progress of gestation is undoubtedly open to criticism. It seems, however, to be the only feasible way of doing it and although there are doubtless errors involved, still the essential point which I believe that my data establish is the S-shaped form of the curve of growth in utero. Now a brief consideration of the probable effect of the above interpolation upon the form of the empirical curve shows that the method employed, far from exaggerating this result, would tend to mask it for the following reasons.

1) It is reasonable to assume that the growth of the placentae and other foetal membranes will keep pace with the growth of the embryos and follow the same curve which would represent their growth. In assuming that the rate of growth is constant, as we have in the method of eliminating their weight, we tend to make the curve of the embryo's growth a straight line and thus straighten out any curved lines which may rightfully be a part of it.

2) What has been said regarding the deciduae may very well be true also of the fat accumulated by the mother during pregnancy. In the light of our present knowledge of hormones and the part they play in life phenomena, especially those connected with reproduction, we may well assume that this accumulation of fat is controlled by internal secretions whose amount and activity in turn are controlled by the growing embryos in utero. In eliminating this fat as if it

Table IV.

Intra-uterine growth of ten litters and the growth of an individual represented by an average.

	A_2	A_3	B_3	B_4	C_4	H_2	X_1	Bp_1	Bp_2	K_1	No. of young	Total weight	Average weight
	No. in litter												
	3	3	2	3	3	3	3	3	3	2			
0	0	0	0	0	0	0	0	0	0	0		0	0
2			17	15	34	−3	16	5	3	19	22	106	4.8
4	25	21	11	0	74	4	28	9	11	−4	25	179	7.1
6	25	3	36	12	53	11	32		10	8	25	190	7.6
8	27	7	47	8	54	28	29	3	8	10	28	221	7.9
10	14	33	51	4	60	17	49		12	9	25	249	9.8
12	21	19	30	3	37	38	31			13	22	192	8.7
14	47	10	30	11		19	40		19	26	22	202	9.2
16		24		20	58	36	38		3	32	20	211	10.5
18	47	32	43	32	55	49	48	12	17	25	28	360	12.8
20	41	30	23	27	52	36	59	7	8	20	28	303	10.8
22	42		36	43	44	35	22	13	35	31	25	301	12.0
24	45		46	28	20	37	18	25	93	35	25	347	13.9
26		45	43	62	62	63	61	25	33	33	25	427	17.1
28	50	42	49	78	64	79	55	24	70	30	28	541	19.3
30	74	71	61	48	66	69	82	44	77	32	28	624	22.4
32	86	57	76	79	74	93	103	34	57	28	28	687	24.5
34	106	66		64	109	107	119	54	84		24	709	29.5
36	107	98	103	98	98	102	103	62	90	75	28	936	33.4
38	128	101	98	158	106	114	119	45	98	85	28	1052	37.6
40	133	78	100	135	157	132	155	79	132	73	28	1164	41.5
42	140	112	117	125	158	113	157	70	114	74	28	1180	42.1
44	172	141	133	136	157	143	167	87	127	75	28	1338	47.8
46	164	131	120	156	165	170	185	96	123	79	28	1389	49.6
48	173	147		145	155	193	173	123	153	91	26	1353	52.0
50	199	154	129	188	164	177	167	124	196	103	28	1601	57.1
52	204	158	136	192	154	186	163	126	202	103	28	1627	58.1
54	213	192	150	189	145	208	160	115	197	110	28	1679	60.0
56	213	205	126	221	152	210	158	130	212	120	28	1747	62.4
58	237	180	146	220	162	218	154	165	210	125	28	1817	64.9
60	184	175	167	245	198	225	146	180	199	126	28	1845	65.8
62	191	145	159	234	184	254	173	178	228	134	28	1880	67.1
64	185	174	143	240	186	246	202	205	226	134	28	1941	69.3
66	195	179	159	256	203	237	204	203	214	164	28	2014	71.9
68	203	203	159	261	233	234	201	228	228	160	28	2110	75.4

increased at a constant rate, we again tend to make the growth curve of the young more nearly resemble a straight line.

3) The hypotenuse of our triangle resembles more closely the growth curve of the mother during the gestation period, for by this time puberty is passed and the growth curve of the mother is approaching an asymptote and is nearly rectilinear.

A few corrections have been made by interpolation in the weights of the pregnant mothers in cases where all the animals were heavy or light due to over- or under-feeding. But this was done only when the difference exceeded twenty grams. In Table IV only 19 out of 314 figures have been thus corrected.

Turning now to the consideration of the curve of intra-uterine growth thus obtained (Fig. 1) certain features of it demand careful attention. The first part of the curve representing the first four days of gestation is not significant of the growth of the fertilized ova but represents the rapid return of the mother to normal weight after the loss occasioned by chasing and copulation. The dotted line, therefore, probably represents the correct course of growth for this period. Although the most rapid cell division and relatively the fastest rate of growth, occurs in the early cleavage stages, still such growth will not be perceptible by the means employed in obtaining this curve. So we should not expect a very rapid increase during the first eight or ten days; for implantation of the ova does not take place till seven days after fertilization[1]). The slight increase in weight shown may be due to the commencement of the accumulation of fat or to other physiological processes in preparation for the coming pregnancy; but this cannot be counted as growth of the litter in utero.

That portion of the curve from ten to sixty days closely resembles other growth curves which represent one cycle of growth. It appears probable, therefore, that one cycle begins at the fertilization of the egg and ends a week or ten days before birth, at which time (or before) another cycle begins and continues on after birth.

In Table V are to be found the weights and average weights for twenty days after birth of the same twenty-eight young whose growth in utero is represented by the first part of the curve. The curve constructed from the averages in Table V is added to the curve at the 68 day ordinate. There is a slight loss of weight at birth

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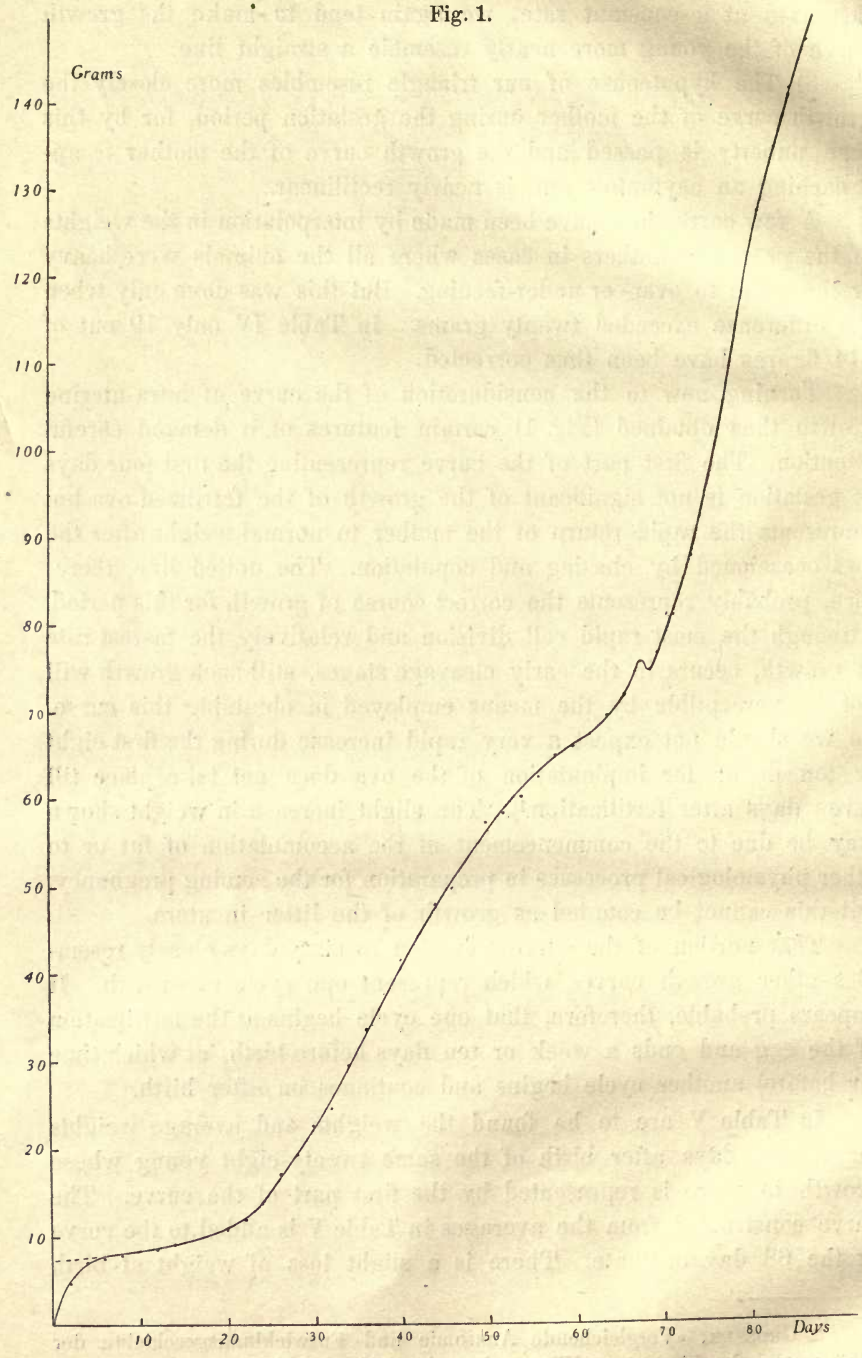
[1]) Grosser, »Vergleichende Anatomie und Entwicklungsgeschichte der Eihäute und der Placenta.« Wien u. Leipzig 1909. S. 162.

Fig. 1.



Intra-uterine growth of the guinea-pig. (Constructed from data in Tables IV and V.)

Table V.

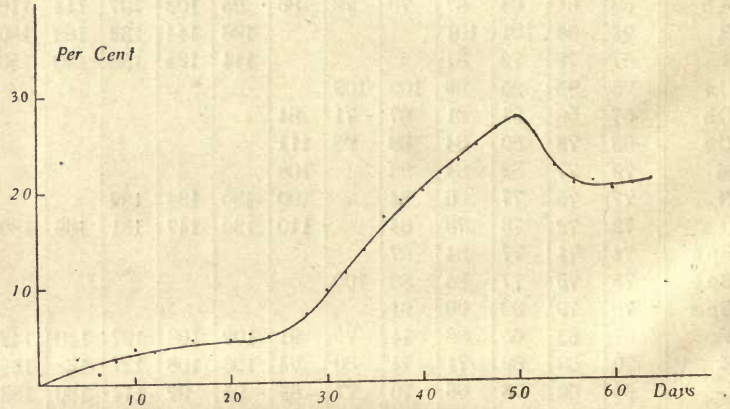
Weights and average weights of the twenty-eight young under consideration, for twenty days following birth.

	Age in days												
	0	1	2	3	4	6	8	10	12	14	16	18	20
G	67	66	65	67	70	75	82	87	97	108	110	116	
H	64	64	63	64	70	77	85	93	105	111	116	123	
I	72	71	70	72	75	84	87	95	107	119	122	133	
W	76	79	82	89	91	102	112	125	122	128	137	133	135
Aa	68	69	74	78	80	91	100	107	118	119	125	132	134
Ab	59	61	63	67	70	78	86	95	102	107	114	118	122
R	92	96	101	101				136	144	162	168	180	182
S	67	72	79	81				114	124	135	139	150	152
Ca	95	93	95	99	102	109							
Cb	57	56	61	61	67	71	84						
Cc	82	76	80	84	88	98	111						
M	79	77	82	84	93		108						
N	77	75	77	80	84		100	130	134	139			
O	72	72	73	78	84		110	136	147	161	166	180	
Bpa	74	74	77	84	87								
Bpb	75	75	77	85	89	100							
Bpc	79	79	82	90	91								
V	67	63	65	68	74	79	91	102	108	127	140	142	160
K	70	66	69	71	74	80	94	106	108	127	138	138	155
L	64	60	63	66	70	77	86	95	99	114	130	133	147
Ka	81	77		83		99	107	119	123	132	144	163	
Kb	79	74		81		98	106	115	117	119	132	140	
Ba	80	79	86	94									
Bb	84	84											
Bc	97	95	101	110									
Hb	76	77		88									
Hc	77	78		84									
Hd	79	81		89									
Number of observations	28	28	22	27	18	15	16	15	15	15	14	14	8
Total	2110	2087	1685	2188	1459	1318	1549	1655	1755	1908	1881	1981	1177
Average	75.4	74.6	76.6	81.0	81.0	87.8	96.8	110.3	117.0	127.2	134.3	141.5	147.1

which is characteristic of almost all mammals, but the animals pick up in two or three days and the curve continues on at the same inclination as the line representing the intra-uterine growth of the last eight or ten days before birth. This fact would seem to indicate that the figures and curve representing the intra-uterine growth, although obtained indirectly, have some degree of accuracy.

Ostwald[1]) in discussing the curve showing the growth of man says, »It is worthy to note again the continuity of the weight changes during the last foetal month and the first years of life. The well known loss of weight of the new born during the first days of life is so insignificant that in comparison to the remaining

Fig. 2.



Curve of pregnancies resulting in abortion (constructed from data in Table VI).

weight changes of the development of man it scarcely needs to be considered«.

It is interesting to note that, as far as we can learn from the data so far obtained, the birth of both guinea-pigs and man does not take place at the juncture of two cycles. This is especially interesting in the case of the guinea-pig, which is born in a very mature state[2]). The period of gestation is very long when we compare it with the gestation period of other rodents. This has led one investigator[3]) to venture the belief that in some remote period in its evolution the guinea-pig was born in a less mature state, such as

1) Ostwald, loc. cit.

2) Read, loc. cit.

3) Abderhalden, »Text-book of Physiological Chemistry.« New York 1908. p. 371.

Table VI.

Per cent of weight gained or lost, during the period of gestation, by five guinea-pigs which gave birth to dead, premature litters.

Days after copulation	Y 7 Born	C 5 Born	A 3 Born	H A 1 Born	K 5 Born	Average per cent increase
0						
2	— 5.8	5.1	0.9	3.0	— 4.4	0.0
4	2.8	— 3.0	5.7	4.4	1.3	2.7
6	0.7	— 0.2	— 3.6	0.0	— 4.7	— 1.5
8	0.7	4.7	— 2.1	— 0.8	2.9	1.1
10	1.0	4.2	0.5	1.0	0.8	1.3
12	0.0	— 1.0	2.0	— 1.2	— 1.6	— 0.5
14	4.0	4.9	— 2.9	2.1	— 0.5	1.5
16	2.5	— 2.0	— 0.7	0.3	— 0.6	— 0.1
18	0.5	— 0.2	0.4	— 7.4	— 2.2	— 1.7
20	0.0	5.1	0.3	1.9	1.2	1.7
22	3.1	— 1.3	2.7	0.1	— 2.0	0.5
24	1.5	— 2.0	— 4.3	1.1	3.4	— 0.2
26	— 3.6	0.7	1.6	— 1.8	2.2	— 0.1
28	2.0	1.2	0.9	5.0	3.8	2.5
30	1.8	3.2	2.0	1.9	4.3	2.6
32	4.8	— 0.7	— 1.0	4.2	1.5	1.7
34	2.5	2.8	3.4	1.1	1.8	2.3
36	2.8	2.4	6.0	4.0	2.8	3.6
38	2.2	0.1	4.6	0.6	0.3	1.7
40	1.5	2.2	— 3.3	1.2	1.3	0.6
42	3.4	1.0	3.0	1.8	1.8	2.1
44	— 0.1	0.7	1.4	1.0	3.0	1.2
46	1.0	2.6	3.2	— 1.6	3.5	1.7
48	— 1.7	3.0	4.4	0.3	4.1	1.8
50	— 5.2	2.0	0.0	1.5	7.6	1.2
52	— 8.0	0.0	0.2	0.0	0.0	— 1.6
54	0.1	— 1.0	— 4.9	— 4.2	— 7.3	— 3.5
56	3.6	— 1.6	— 4.2		— 5 3	— 1.9
58	0.4	— 4.3	4.6		0.9	0.4
60	1.0	— 2.5				— 0.7
62	1.0	— 0.4				0.3
64		— 0.5				— 0.5

that in which rabbits, mice, and rats are born. If such were the case, the young must have been born before 50 days, for the two cycles seem to join or overlap between 50 and 60 days. This period seems to be a critical one in the development of the foetus. Inspection of the weights of mothers which gave birth to dead young

shows that these mothers lost weight rapidly during this period. Table VI gives the percentage of weight gained or lost every second day by five mothers who gave birth to premature, dead litters. Fig. 2 shows the curve constructed from this data. A distinct loss of weight is shown after 50 days. Whether or not this phenomenon has any connection with growth cycles, it is impossible now to say with certainty. But it is possible that the death of the young in utero may be due to a failure of the second cycle to connect properly with the first. The fact of the death in utero at this period is undeniable and I mention it as possibly having some significance and bearing upon this and perhaps other questions of intra-uterine development.

In conclusion, I may say that I realize fully the fact that the data upon which the curve has been constructed have been obtained indirectly and that more accurate data could be obtained only by the sacrifice of hundreds of animals. But as a first attempt to arrive at the truth in regard to the appearance of a curve representing the growth following fertilization, I it submit with the hope that it may serve as a starting point for further work.

Summary and Conclusions.

From the facts and figures set forth and discussed in this paper and from the appearance of the curve constructed from the data, it seems reasonable to conclude that:

I. It is possible to obtain a curve showing the growth of embryos in utero by indirect means, i. e. by weighing the mother at regular intervals during pregnancy.

II. In the case of guinea-pigs, one cycle begins at fertilization of the ova and ends about 60 days after. Another cycle begins a little before the end of the first cycle and continues on after birth.

III. In both the guinea-pig and man birth occurs during the course of a cycle and not at or near the juncture of two cycles.

IV. The human young are born before the completion of the first cycle, while the guinea-pig completes one cycle and begins a second in utero. It is quite likely that this fact accounts for the advanced state of development of the latter animal at birth.

Zusammenfassung.

Nach den in dieser Arbeit vorgebrachten und erörterten Figuren und Tatsachen und nach dem Aussehen der aus diesen Tatsachen konstruierten Kurve scheinen mir nachstehende Schlußfolgerungen erlaubt:

1) Es ist möglich, eine Kurve zu erhalten, welche das intrauterine Wachstum von Embryonen durch indirekte Mittel veranschaulicht, so durch regelmäßig wiederholte Wägung der Mutter in regelmäßigen Zwischenräumen während der Schwangerschaft.

2) Für das Meerschweinchen beginnt ein Zyklus bei der Befruchtung der Eier und endet ungefähr 60 Tage später. Ein andrer Zyklus beginnt eine kleine Weile vor dem Ablauf des ersten Zyklus und dauert noch nach der Geburt an.

3) Sowohl beim Meerschweinchen wie beim Menschen fällt die Geburt in den Verlauf eines Zyklus und nicht in oder nahe an die gemeinsame Ablaufszeit zweier Zyklen.

4) Die Jungen des Menschen werden noch vor der Vollendung des ersten Zyklus geboren, während das Meerschweinchen noch im Uterus einen Zyklus vollendet und einen zweiten anfängt. Es ist durchaus wahrscheinlich, daß dieser Umstand die Ursache für das vorgerückte Entwicklungsstadium des letzteren Tieres bei der Geburt abgibt.

(Übersetzt von **W. Gebhardt.**)

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Atlas zur Entwicklungsgeschichte des menschlichen Auges

von

Ludwig Bach und **R. Seefelder**
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